REMARKS

Claims 1-25 are pending before entry of this amendment.
Claims 7-19 are withdrawn.
Claims 1-6 and 10-25 are rejected.
Please amend claim 1 as follows.

Generally

Applicants have considered the examiner's arguments and thank the examiner for her clarity. The applicants believe that they understand the examiners rejections of the previously pending claims in view of Manning and Hussman, and, while still maintaining the previous arguments, have amended and further limited the claims in a way which, applicants believe, distinguishes the presently claimed invention form either (or any combination of) the cited references.

Particularly, Manning, which is the mainstay of the examiner's arguments, discloses the use of a Hyaluronic Acid (HA) gel to deliver gentamicin to the middle ear. This HA delivery system, according to Manning, delivers the drug for a short period of not more than about 24 hours. See page 10, lines 1-13 where Manning teaches "the drug is nearly completely delivered (about 75%) by 24 hours." and that "...by 24 hours, the total amount released is approximately 80-90%." Also, Manning, at page 5, states that "In the laboratory, the gel appears to be liquid enough to disappear from the site within seven to ten days with minimal agitation."

From Manning's own words, it seems clear that the HA system described is not suitable for the delivery of a drug for a period of more than about 24 hours. Because of this, Manning would not anticipate or make obvious an invention that delivers drug for a sustained period of more than about 24 hours.

The applicants have thus amended the claims to recite a "method for delivering therapeutic agents ... for a period of greater than a month, said method comprising...allowing said drug delivery unit in said round window niche to release said therapeutic agent...wherein said therapeutic agent is released over a period of greater than one month." Applicants believe that the present amendments overcome the rejections under 35 USC 102 and 35 USC 103.

Rejections under 35 USC §102

Claims 1, 3, 4, 6, 20, and 22-25 (not claims 2, 5, or 21) are rejected under 35 USC §102(a) as anticipated by Manning et al. Applicants rebut the rejection on the grounds that the reference does not teach a method for delivering therapeutic agents ... for a period of greater than a month, said method comprising...allowing said drug delivery unit in said round window niche to release said therapeutic agent...wherein said therapeutic agent is released over a period of greater than one month.

An anticipatory reference must teach and every element of the claimed invention is not taught or implied by the reference (MPEP at 706.02):

> "...for anticipation under 35 USC 102, the reference must teach each and every aspect of the claimed invention either explicitly or impliedly. Any feature not inherently taught must be inherently present."

In the present case, Manning neither teaches nor suggests teach a method for delivering therapeutic agents for a period of greater than a month, said method comprising...allowing said drug delivery unit in said round window niche to release said therapeutic agent...wherein said therapeutic agent is released over a period of greater than one month.

In contrast, Manning discloses the use of a Hyaluronic acid gel, wherein "the drug is nearly completely delivered (about 75%) by 24 hours." (See Manning, page 10, lines 1-13) and further, wherein "...by 24 hours, the total amount released is approximately 80-90%." Also, Manning, at page 5, states that "In the laboratory, the gel appears to be liquid enough to disappear from the site within seven to ten days with minimal agitation." Clearly, the device of Manning could not anticipate or make obvious an invention that delivers drug for a sustained period of more than about 24 hours, more particularly more than one month, as claimed.

Rejections under 35 USC §103

Claims 1, 2, 4, 5, and 20-21 (not 3, 6, or 22-25) are rejected as obvious over Manning et al in view of Hussman et al.

Applicants rebut the rejection on the grounds that a prima facie case has not been established because there would be no reasonable expectation of success in practicing the presently claimed invention if Manning et al and Hussman et al were combined (MPEP at 706.02(j)):

> "To establish a prima face case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation ...to modify or combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not [be] based on applicant's disclosure. In re Vaeck, 947 F.2d 488; 20 USPQ2d 1438 (Fed. Cir. 1991)."

Manning discloses **the short-term delivery** of a drug using a Hyaluronic acid gel, wherein "the drug is nearly completely delivered (about 75%) by 24 hours." (See Manning, page 10, lines 1-13) and further, wherein "...by 24 hours, the total amount released is approximately 80-90%."

Hussman discloses Gelfoam, a specially treated porcine-derived gelatin product to deliver gentamicin to the ear for the purpose of **causing nerve damage**.

One of skill in the art would not and could not combine the inventions of Manning and Hussman to make obvious a method for treating a disease by delivering therapeutic agents for a period of greater than a month...wherein said therapeutic agent is released over a period of greater than one month.

The Manning disclosure has already been discussed.

Looking at the Hussman disclosure, the quantity of gentamicin delivered, rate of delivery, and the method of delivery required for a *therapeutic* purpose is diametrically different from that required to *cause nerve damage*, therefore the Hussman reference, in combination with Manning, cannot make the current invention obvious, since it teaches a method that would *not* enable one of skill in the art to practice the current invention with a *reasonable expectation of success*. In fact, since Husmann teaches nerve damage to the ear by the delivery of gentamicin using Gelfoam, one could reasonably suggest that the reference *teaches away* from the current invention – certainly from using Gelfoam (though applicants do not believe that the assertion of teaching away is germane here, since Gelfoam is not equivalent to the synthetic controlled release carrier material of the present invention).

Such potential damage is additionally supported by explicit reference in product literature (supplied by Upjohn, the Gelfoam manufacturer) to adverse reactions caused when Gelfoam is used during tympanoplasty (see EXHIBIT B of previously filed response). These adverse reactions include hearing loss. Clearly this would act as a disincentive to one of skill in the art to use Gelfoam as a material to deliver a therapeutic agent to the middle ear. Additionally, Gelfoam has been shown to be associated with fibrosis, neovascularization and epithelial metaplasia of the round window membrane when used for grafting (EXHIBIT C of previously filed response). Thus the Husmann reference cannot, in combination with Manning, make obvious the present invention. In view of the above facts and reasoning, applicants respectfully suggest that one of skill in the art would not and could not combine the inventions of Manning and Hussman to make obvious a method for treating a disease by delivering therapeutic agents for a period of greater than a month...wherein said therapeutic agent is released over a period of greater than one month, and thus request that the rejections under 35 USC §103(a) be withdrawn.

In light of the above amendments and remarks, applicants submit that the present application is fully in condition for allowance, and request that the examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, applicants invite the examiner to contact applicants' attorney at (408) 864-7435.

Applicants believe that a 2 month Extension of Time fee is due with this communication, and requests that it be debited from the deposit account No. **50-1953**. The Commissioner is hereby authorized to charge any additional fees required under 37 C.F.R. § 1.16 and 1.17, or credit any overpayment to Deposit Account No. **50-1953. A duplicate of this sheet is enclosed.**

Respectfully submitted,
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Version with markings to show changes made

1. **(Once Amended)** A method for treating a disease by delivering therapeutic agents into the inner ear of a living subject through the round window niche and the round window membrane thereof, for a period of greater than a month, said method comprising:

providing a drug delivery unit comprised of at least one synthetic controlled release carrier media material and at least one therapeutic agent combined therewith, said carrier media material releasing said therapeutic agent from said drug delivery unit over time when said drug delivery unit is placed in said round window niche of said subject;

placing said drug delivery unit at least partially in said round window niche of said subject; and

allowing said drug delivery unit in said round window niche to release said therapeutic agent therefrom so that said therapeutic agent comes in contact with said round window membrane, passes therethrough, and enters said inner ear, wherein said therapeutic agent is released over a period of greater than one month.

2. (Reiterated) The method of claim 1 wherein said drug delivery unit is spaced apart from said round window membrane in said round window niche.

3. (Reiterated) The method of claim 1 wherein said drug delivery unit is positioned against and in direct contact with said round window membrane in said round window niche.

4. (Reiterated) A method for delivering therapeutic agents into the inner ear of a living subject through the round window niche and the round window membrane thereof, said method comprising:

providing a drug delivery unit comprised of at least one biodegradable controlled release carrier media material and at least one therapeutic agent combined therewith, said carrier media material releasing said therapeutic agent from said drug delivery unit over time when said drug delivery unit is placed in said round window niche of said subject;

placing said drug delivery unit at least partially in said round window niche of said subject; and

allowing said drug delivery unit in said round window niche to release said therapeutic agent therefrom so that said therapeutic agent comes in contact with said round window membrane, passes therethrough, and enters said inner ear.

5. (Reiterated) The method of claim 4 wherein said drug delivery unit is spaced apart from said round window membrane in said round window niche.

6. (Reiterated) The method of claim 4 wherein said drug delivery unit is positioned against and in direct contact with said round window membrane in said round window niche.

7. (Withdrawn) A method for delivering therapeutic agents into the inner ear of a living subject through the round window niche and the round window membrane thereof, said method comprising:

providing a drug delivery apparatus comprising:

an elongate member comprising a first end and a second end; and

a drug delivery unit secured to said first end of said elongate member, said drug delivery unit being comprised of at least one controlled release carrier media material and at least one therapeutic agent combined therewith, said carrier media material releasing said therapeutic agent from said drug delivery unit over time when said drug delivery unit is placed in said round window niche of said subject;

placing said first end of said elongate member and said drug delivery unit secured thereto at least partially in said round window niche of said subject; and

allowing said drug delivery unit in said round window niche to release said therapeutic agent therefrom so that said therapeutic agent comes in contact with said round window membrane, passes therethrough, and enters said inner ear.

8. (Withdrawn) The method of Claim 7 wherein said elongate member comprises a solid rod.

9. (Withdrawn) The method of Claim 7 wherein said elongate member comprises at least one passageway therethrough from said first end to said second end.

10. (Withdrawn) The method of Claim 7 wherein said elongate member is comprised of at least one electrically conductive material.

11. (Withdrawn) The method of Claim 7 wherein said carrier media material is biodegradable.

12. (Withdrawn) A method for delivering therapeutic agents into the inner ear of a living subject through the round window niche and the round window membrane thereof, said method comprising:

providing a drug delivery apparatus comprising:

an elongate electrically conductive member comprising a first end and a second end; and

a drug delivery unit secured to said first end of said conductive member, said drug delivery unit being comprised of at least one controlled release carrier media material and at least one therapeutic agent combined therewith, said carrier media material releasing said therapeutic agent from said drug delivery unit over time when said drug delivery unit is placed in said round window niche of said subject;